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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,479	10/05/2006	Narito Tateishi	Q94241	2355

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2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

EXAMINER	
CARTER, KENDRA D	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
12/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/574,479	TATEISHI ET AL.	
	Examiner	Art Unit	
	KENDRA D. CARTER	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,22 and 25-45* is/are pending in the application.

4a) Of the above claim(s) *22,36 and 2535* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,26-34 and 37-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/3/06;1/2/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 21 and 26-44, and species election of (2R)-2-propyloctanoic acid as the fatty acid, differentiation as the type of nerve regeneration and nerve cell as the type of cell in the reply filed on July 22, 2009 is acknowledged. Thus, claims 22, 25, 35 and 36 are withdrawn as being drawn to non-elected groups or species. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1) Claims 21 and 26-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nerve regeneration with (2R)-2-propyloctanoic acid, does not reasonably provide enablement for <u>any</u> fatty acid compound and its prodrug thereof. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of acceleration nerve regeneration comprising administering an effective amount of any fatty acid compound and its prodrug thereof. The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 21 is drawn to "a method for accelerating nerve regeneration in a mammal, which comprises administering to a mammal an effective amount of a fatty acid compound, a salt thereof or a prodrug thereof, provided that the fatty acid compound Is not retinoic acid or a prostaglandin compound." Claim 26 is drawn to "the method according to claim 21, wherein the fatty acid compound is an unsaturated fatty

acid compound." Claim 27 is drawn to "the method according to claim 21, wherein the fatty acid compound is a saturated fatty acid compound." Claim 28 is drawn to "the method according to claim 21, wherein the fatty acid compound is a branched chain fatty acid compound." Claim 29 is drawn to "the method according to claim 21, wherein the fatty acid compound is a linear or branched chain fatty acid compound having from 4 to 20 carbon atoms." Claim 30 is drawn to "the method according to claim 21, wherein the fatty acid compound is represented by formula (I): wherein R.sup.1 represents hydroxyl; R.sup.2 and R.sup.3 each independently represents (a) hydrogen, (b) chlorine, (c) C3-10 alkyl, (d) C3-10 alkenyl, (e) C2-10 alkoxy, (f) C2-10 alkylthio, (g) C3-7 cycloalkyl, (h) phenyl, (i) phenoxy, (j) (C2-10 alkyl substituted with one or two chorine atom(s))-CH.sub.2--, (k) (C1-5 alkyl substituted with one or two substituent(s) selected from C1-4 alkoxy, C3-7 cycloalkyl, phenyl and phenoxy)-CH.sub.2--, (1) (C1-10 alkyl in which one carbon atom is substituted with 1 to 3 fluorine atom(s))-CH.sub.2--, or (m) oxidized C3-10 alkyl, or R.sup.2 and R.sup.3 are taken together to represent C3-10 alkylidene; and R.sup.4 represents C2-3 alkyl or oxidized C2-3 alkyl." Claim 31 is drawn to "the method according to claim 30, wherein the fatty acid compound is (1) 2-propyloctanoic acid, (2) (2R)-2-propyloctanoic acid, (3) (2S)-2-propyloctanoic acid, (4) 2-propylpentanoic acid, (5) (2R)-7-oxo-2-propyloctanoic acid, (6) (2R,7R)-7-hydroxyl-2-propyloctanoic acid, (7) (2R,7S)-7-hydroxyl-2-propyloctanoic acid, or (8) (2R)-8-hydroxyl-2-propyloctanoic acid."

(2) The breadth of the claims:

Claims 21 and 26-31 embraces and reads on effectively accelerating nerve regeneration in a mammal with any fatty acid compound and its prodrug. The specification does not enable the effective acceleration of nerve regeneration with any fatty acid compound and its prodrug.

(3) The state of the prior art:

The state of the art regarding effectively regenerating nerves with any fatty acid compound is very low. Laeng et al. (W) 02/102989 A2) teach that valproate promotes neurogenesis, neurite outgrowth of neurons in brain stem cells (see page 38), inhibits the differentiation of cortical stem cells into astrocytes, and increases the differentiation of cortical stem cells into GABA expressing cells (see page 39).

(4) The predictability or unpredictability of the art:

The predictability of accelerating nerve regeneration in a mammal with any fatty acid compound and its prodrug is relatively low. Therefore, to one skilled in the art, accelerating nerve regeneration in a mammal with any fatty acid compound and its prodrug is unpredictable. In other words, just because there are potential in regenerating nerves with any fatty acid, effective regeneration has yet to be completely established. As Laeng et al. teaches, valproate can promote nerve growth, but not all fatty acid, nor their prodrugs. Therefore, because there is a "potential", accelerating nerve regeneration with any fatty acid and its prodrug is unpredictable.

(5) The relative skill of those in the art:

The relative skill in the art is fairly high, with the typical practitioner having a medical degree and/or an advanced degree in the biology, biochemical, chemistry or pharmaceutical-related arts, as evidenced by Laeng et al.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to accelerating nerve regeneration in a mammal with any fatty acid compound and its prodrug is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that accelerate nerve regeneration with any fatty acid compound ant its prodrug. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02. Particularly, the specification teaches that (2R)-2-propyloctanoic acid regenerates brain nerve cells (see page 36, lines 1-15). There are no further tests with a subset of fatty acids that effectively regenerate nerve cells. The specification defines prodrugs of formula I to be either a hydrate or a non-hydrate (see page 17, lines 12-14). There is no description or examples of any prodrugs of formula I, nor its effective activity.

(7) The quantity of experimentation necessary:

The instant claims read on accelerating nerve regeneration in a mammal with any fatty acid compound and its prodrug. As discussed above the specification fails to provide any support for accelerating nerve regeneration in a mammal with any fatty acid compound and its prodrug. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation.

Particularly, the skilled practitioner would have to test each and every one of compounds as claimed, or at least a subset that is sufficiently representative of the compounds, to determine regeneration efficacy. For example, the compound would have to be obtained through synthesis or bought and then tested to see if it accelerated nerve regeneration in a mammal. If efficacy of the drug did not result, the dosage regime would have to be varied, for example by changing the dosage amount or route of administration, until efficacy was achieved. If efficacy in the treatment of the condition was shown with the particular compound, then another compound would have to be selected and the process would have to be repeated, including determining the optimum dosage regimen and toxicity levels for evaluation. Thus, the skilled artisan would have to undergo exhaustive studies to evaluate each compound, in order to be able to fully carry out the invention commensurate in scope with the claims.

Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent

protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for accelerating nerve regeneration in a mammal with (2R)-2-propyloctanoic, but not for any fatty acid compound and its prodrug.

2) Claims 21 and 40-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nerve regeneration with (2R)-2-propyloctanoic acid of a cerebral nerve, does not reasonably provide enablement for the regeneration of any nerve. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to a method of acceleration nerve regeneration comprising administering an effective amount of a fatty acid compound. The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the invention:

The claim 21 is drawn to "a method for accelerating nerve regeneration in a mammal, which comprises administering to a mammal an effective amount of a fatty acid compound, a salt thereof or a prodrug thereof, provided that the fatty acid compound Is not retinoic acid or a prostaglandin compound." Claim 40 is drawn to "the method according to claim 21, wherein the nerve is a central nerve or a peripheral nerve." Claim 41 is drawn to "the method according to claim 40, wherein the central nerve is a cerebral nerve, a spinal nerve or an optic nerve." Claim 42 is drawn to "the method according to claim 40, wherein the peripheral nerve is a motor nerve or a sensory nerve."

(2) The breadth of the claims:

Claims 21 and 40-42 embraces and reads on effectively accelerating any nerve regeneration in a mammal with any fatty acid compound and its prodrug. The specification does not enable the effective acceleration of any nerve regeneration with any fatty acid compound and its prodrug.

(3) The state of the prior art:

The state of the art regarding effectively regenerating any nerve with any fatty acid compound is very low. Laeng et al. (W) 02/102989 A2) teach that valproate promotes neurogenesis, neurite outgrowth of neurons in brain stem cells (see page 38), inhibits the differentiation of cortical stem cells into astrocytes, and increases the differentiation of cortical stem cells into GABA expressing cells (see page 39).

(4) The predictability or unpredictability of the art:

The predictability of accelerating nerve regeneration in a mammal with any fatty acid compound and its prodrug is relatively low. Therefore, to one skilled in the art, accelerating nerve regeneration in a mammal with any fatty acid compound and its prodrug is unpredictable. In other words, just because there are potential in regenerating nerves with any fatty acid, effective regeneration has yet to be completely established. As Laeng et al. teaches, valproate can promote nerve growth, but not all fatty acid, nor their prodrugs. Therefore, because there is a "potential", accelerating any nerve regeneration with any fatty acid and its prodrug is unpredictable.

(5) The relative skill of those in the art:

The relative skill in the art is fairly high, with the typical practitioner having a medical degree and/or an advanced degree in the biology, biochemical, chemistry or pharmaceutical-related arts, as evidenced by Laeng et al.

(6) The amount of direction or guidance presented / working examples:

In the instant case, the guidance of the specification as to accelerating any nerve regeneration in a mammal with any fatty acid compound and its prodrug is completely lacking. The specification as filed does not speak on or show any working examples any studies performed that accelerate any nerve regeneration with any fatty acid compound ant its prodrug. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.02. Particularly, the specification teaches that (2R)-2-propyloctanoic acid regenerates brain nerve cells (see page 36, lines 1-15). There are no further tests with a subset of fatty acids that effectively regenerate other types of nerve cells such as peripheral, spinal or optic nerves.

(7) The quantity of experimentation necessary:

The instant claims read on accelerating any nerve regeneration in a mammal with any fatty acid compound and its prodrug. As discussed above the specification fails to provide any support for accelerating any nerve regeneration in a mammal with any fatty acid compound and its prodrug. Applicant fails to provide any information sufficient to practice the claimed invention, absent undue experimentation.

Particularly, the skilled practitioner would have to test each and every one of compounds as claimed, or at least a subset that is sufficiently representative of the compounds, with a subset of central and peripheral nerves to determine regeneration

efficacy. For example, the compound would have to be obtained through synthesis or bought and then tested to see if it accelerated central and peripheral nerve regeneration in a mammal. If efficacy of the drug did not result, the dosage regime would have to be varied, for example by changing the dosage amount or route of administration, until efficacy was achieved. If efficacy in the treatment was shown with the particular compound, then another compound and type of nerve would have to be selected and the process would have to be repeated, including determining the optimum dosage regimen and toxicity levels for evaluation. Thus, the skilled artisan would have to undergo exhaustive studies to evaluate each compound and type of nerve cell, in order to be able to fully carry out the invention commensurate in scope with the claims.

Genetech, 108 F. 3d at 1366 states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimation of general ideas that may or may not be workable.

In conclusion, the applicant is enabled for accelerating cerebral nerve regeneration in a mammal with (2R)-2-propyloctanoic, but not for any fatty acid compound and its prodrug to regenerate any nerve.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21, 26-34, 37-41, 44 and 45 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohuchida et al. (US 6,201,021 B1).

Ohuchida et al. teach pentanoic acid derivatives such as 2-propylocanoic acid (see claim 9) that treat neurodegenerative diseases and neuronal dysfunction by stroke or traumatic injury (see abstract; addresses claims 21, 26-32 and 45). Since 2-propylocanoic acid has both the (R) and (S) enantiomer, the Examiner reads that (2R)-2-propylocantoic acid is present. Particularly, the pentanoic acid derivatives elicited potent effects in improving astrocyte functions (see column 27, experiment 1, table 1, lines 40-55; addresses claims 21, 33, 44 and 45), elicited marked regeneration effects of GABA receptor responses against reactive astrocytes wherein the compounds are effective in transforming reactive astrocytes to astrocytes (i.e. acceleration differentiating nerve cell; see columns 27 and 28, tables 2 and 3, lines 63-67; addresses claims 21, 44 and 45) and suppressive effects on on-cell death in symbiotic neurons-astrocytes wherein dendrite generation in the neurons were detected (see column 29, lines 1-31; addresses claims 21, 44 and 45). The astrocyte cultures were isolated from

cerebrums of neonatal rats (see column 27, lines 13-18; addresses claims 37-41 and 45).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ohuchida et al. (US 6,201,021 B1) as applied to claims 21, 26-34, 37-41, 44 and 45 above in view of Mazo (Pittsburgh Post Gazette, April 12, 2000, pages 1-3).

The teaching of Ohuchida et al. are as applied above for claims 21, 26-34, 37-41, 44 and 45.

Ohuchida et al. does not teach that the cells are for transplant.

Mazo teach that brain cell transplants are known to be successful for the treatment of stroke (see page 1).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the teaching of Ohuchida et al. and to transplant the regenerated nerve cells because it has been successfully used in the treatment of stroke.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 9:00 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kendra D Carter/
Examiner, Art Unit 1627

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627